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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,610	09/16/2003	**Charles Wilson**	23239-538 (ARC-38)	5499

30623 7590 10/28/2008

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY AND POPEO, P.C
ATTN: PATENT INTAKE CUSTOMER NO. 30623
ONE FINANCIAL CENTER
BOSTON, MA 02111

EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	**PAPER NUMBER**
1648	

MAIL DATE	DELIVERY MODE
10/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,610	WILSON ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *46-57,60-64,66,69-111 and 113-126* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46-57,60-64,66,69-111 and 113-126* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04 August 2008 has been entered.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

DETAILED ACTION

This Office Action is in response to the amendment filed 4 August 2008. Claims 1-45, 58, 59, 65, 67, 68 and 112 have been cancelled. Claims 46-57, 60-64, 66, 69-111 and 113-126 are pending and currently examined.

Claim Objections

The objection to claim 114 is withdrawn in response to Applicant's amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 46-57, 60-64, 66, 69-111 and 113-126 under 35 U.S.C. §103(a) as being obvious over Griffin *et al.* (U.S. Patent No. 5,756,291, hereinafter "Griffin") is **maintained** for reasons of record.

The instant invention is a method for identifying an aptamer that binds to a target, wherein binding of the aptamer to the target increases the binding affinity of the target for a target partner, comprising:

a) contacting a mixture of nucleic acids with the target partner (TP) or target partner analog (TPA) or both;

b) partitioning the bound nucleic acids from the unbound nucleic acids and retaining the unbound nucleic acids;

c) contacting the unbound nucleic acids with the target and the TP or TPA or both;

d) partitioning bound nucleic acids from unbound nucleic acids; and

e) retaining the bound nucleic acids.

Griffin describes a method for identifying aptamers that specifically bind to a target, such as a cell surface molecule or glycoprotein (Abstract and col. 13, lines 40-47), comprising:

(a) contacting (incubating) a pool of oligonucleotides with support-bound target molecules;

(b) partitioning (detaching) the resulting target-oligonucleotide complexes from the support (see col. 1, lines 32-59);

Griffin describes selection of aptamers that bind to surface antigens, involving a procedure wherein negative selection (similar to the claimed steps (a)-(b) retaining unbound oligonucleotides) is first carried out, wherein non-specific aptamers can be eliminated by their binding to non-target surfaces, followed by a positive selection (similar to the claimed steps (c)-(e) retaining bound oligonucleotides) by combining the oligonucleotides which did not bind to the non-target molecules thereon with a cell culture containing the target molecule on their surface (see the paragraph bridging columns 29-30). The bound aptamer population is recovered and amplified (see col.

29, lines 17-27), which is claimed in claims 51 and 52. Griffin also discloses that glycoproteins, proteins, carbohydrates, membrane structures, receptors, organelles, and the like can be used as the complexation targets. See column 13, lines 25-27. Most relevantly, Griffin descrives an approach wherein a pool of oligonucleotides is subjected to two rounds of selection. The first round involves selecting oligonucleotides that bind to thrombin, a single molecule target. The second round involves selecting those oligonucleotides that bind to a complex between a target (thrombomodulin) and a target partner (thrombin) (see col. 24, lines 1-13), which is the same as the claimed target complex. Griffin further discloses eluting the bound aptamers with an agonist competitor such as fibrinogen immobilized on a column (column 23, lines 49-51) for further negative selection, which is claimed in claims 53 and 55. The pool of nucleic acids are immobilized on beads (column 23, line 54). Therefore, Griffin describes a method for identifying aptamers that bind to a target like thrombin and increase the binding of thrombin with its partner, thrombomodulin.

Although Griffin does not disclose the exact selective property and the exact order of method steps as claimed, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the thrombin/thrombomodulin complex aptamers selection method disclosed by Griffin using the negative-positive aptamer selection suggested by Griffin, so that only the unbound oligonucleotides from the first round is used in the second round of selection and the thrombin/thrombomodulin complex-bound oligonucleotides are retained. The skilled

artisan would have been motivated to do so to develop complex-favoring aptamers that function as an agonist that delivers the therapeutic ligand to the specific desired receptor and enhance the binding between the ligand and the receptor. There would have been a reasonable expectation of success, given the general protocol of aptamer negative-positive selection protocol with suggested variations (col. 23, line 66 to col. 24, line 13) to obtained desired aptamers and the teaching that a wide variety of materials, including cell surface glycoproteins, can serve as targets, as taught by Griffin. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments have been fully considered but are not persuasive. Applicant argues that Griffin does not disclose the claimed method for identifying aptamers regulators that facilitate the binding of the target to the target partner. Rather, Griffin discloses a method for identifying an aptamer that binds to a pre-existing protein complex between thrombin and thrombomodulin. However, Applicant has not provided any evidence showing that an aptamer binding to a pre-existing complex between thrombin and thrombomodulin would not facilitate the binding. Since the selection steps are similar to the claimed method steps, one skilled in the art would expect the same result as the claimed method, which is to obtain complex-facilitating aptamers. Examiner agrees with the Applicant that the Griffin patent does not disclosed

the claimed method word-for-word. However, Applicant has not presented any reasoning to show nonobviousness of the rejection at issue. Griffin discloses general approaches involving the use of multiple selections to derive aptamers with highly specific properties (col. 24, line 2-4). The method is not limited by the specific examples set forth in the Griffin patent. Even though the aptamer identification method does not select for exactly the same property as the claimed invention, it would be obvious to one skilled in the art at the time to modify the functional selection methods by variations with the target in each binding step and the product in the retaining step to identify aptamers with the desired property.

Applicant further argues that Griffin does not describe eluting the bound aptamers with an agonist competitor. Examiner does not concur. The limitation of "elution" is encompassed by the term "recovery" in the Griffin patent. Griffin discloses elution by describing recovering bound aptamers with one or more of a number of agents (col. 30, lines 29-31). Griffin provides the general guideline of "mixing the oligonucleotide mixture with the undesired substance," which would be the complex of target/partner *under favoring conditions* in the instant invention, "to complex away the members of the oligonucleotide mixture which bind to the second substance," which is the complex of target/partner *under disfavoring conditions* in the instant invention; the uncomplexed oligonucleotides are then recovered and amplified and incubated with the target under conditions wherein those members of the oligonucleotide mixture which bind targets are complexed. The resulting complexes then removed from the

uncomplexed oligonucleotides and the bound aptamers population is recovered and amplified (col. 29, lines 17-27). It would be obvious and within knowledge of one skilled in the art to apply the Griffin aptamers selection method to select for any other desired property.

Applicant argues that a modification to the Griffin method would render it unsatisfactory for its intended purpose. However, this argument mischaracterizes the rejection because Griffin *et al.* was offered for disclosing an obvious variant of the claimed method with different selection conditions. The instant rejection under 35 U.S.C. 103(a) does not require the reference to teach every limitation and every method exactly as recited in the claimed invention, otherwise this rejection would be under 35 U.S.C. 102. Furthermore, Applicant admits that the Griffin method may identify an agonist aptamers or an aptamers regulator by chance, which contradicts Applicant's assertion of the lack of a reasonable expectation of success.

Applicant further asserts that there is a big difference between identifying an aptamer and identifying an agonist aptamer. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., agonist aptamer or aptamer regulator) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant lastly argues that Griffin only teaches a method for selecting an aptamer that binds to thrombin using the basic selection method and then evaluating

the aptamers for the additional property of agonist activity that purely presents as a matter of chance. However, the claimed iterative method steps, i.e. contacting (or incubating) a candidate mixture of nucleic acids (or a pool of oligonucleotides) with the target (be it desired or undesired, hence the term negative or positive selection), partitioning the bound nucleic acids from the unbound nucleic acids, and then to either remove the nonspecific nucleotides by retaining unbound nucleotides or obtain the specific desired nucleotides by retaining bound nucleotides, are specifically described by Griffin *et a*l. The claimed invention does not distinguish from the prior art selection method steps and certainly does not contain specific limitations, such as specific conditions favoring and disfavoring complex formation, that are crucial for the claimed property selection method. Therefore, a case of prima facie obviousness is properly established.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/L. H./
Examiner, Art Unit 1648

/Jeffrey S. Parkin, Ph.D./
Primary Examiner, Art Unit 1648

23 October 2008